

RESULTS FOLLOWING THE EXTIRPATION OF THE PINEAL GLAND IN NEWLY HATCHED CHICKS

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FOUR FIGURES

The prevailing notion of the function of the pineal gland attributes to this organ the elaboration of an internal secretion which inhibits the growth of the body and the development of the mind as well as the primary and secondary sexual characteristics from exceeding a rate which is regarded as normal for preadult life. This rather definite statement of the function of this organ has been an outgrowth from chiefly two sources: from clinical evidence apparently resulting from tumors of the pineal gland and from experimental results. There are those who, in view of the fact that some clinical evidences admit of a varied interpretation and that experimental results have often been contradictory, claim that the function of this organ is not known. The view has also been expressed (Krabbe, '23) that, on account of the varied structure of this organ in different vertebrates, there can exist some variation in function. There are also still those who look upon the pineal gland as a rudimentary organ without any functional significance.

The results obtained by some investigators from the extirpation of the pineal gland lend support to the prevailing notion of its function. These confirmatory results have, however, been in part or entirely discredited by similar experiments of other investigators. Apparently due to technical difficulties, only a comparatively few investigators have attempted the extirpation experiments. Additional data on

the results of this method of experimentation are, therefore, deemed desirable.

Exner and Boese ('10) both transplanted and extirpated the pineal gland of young rabbits. The transplants were speedily absorbed without influence on the host. By means of thermocautery they attempted the destruction of the pineal gland in ninety-five young rabbits. Seventy-three of these died from hemorrhage within twelve hours after the operation. Twenty-two animals survived the operation and were observed for some time without any change from the normal. Six of these (three males and three females) reached sexual maturity. Subsequent microscopic examination proved the complete destruction of the gland. They observed no evidence of a premature maturity and concluded that the destruction of the gland in rabbits produced no noticeable effects.

Biedel ('13) obtained negative results from the extirpation of the pineal gland in adult animals.

Foa ('12) extirpated the pineal gland from sixty-three chicks ranging from eleven to thirty days in age. Fifteen (three cockerels and twelve hens) survived the operation. The growth of the body of the cockerels was retarded during the first two or three months following the operation, but after this period of retarded growth they attained the weight of the normal adults and remained within the limits of normal adult size. In the cockerels the primary and secondary sex characters (sexual instinct, crowing, comb) were manifested sooner than in the control cockerels. Eight to eleven months after the operation it was found that the testes and comb were considerably hypertrophied. No noticeable effect was produced on the operated hens. Hence, he claims that his experiment demonstrates that apinealism results in a precocious and exaggerated development of the primary and secondary sexual characters of the males.

Foa ('14) repeated the experiment. He extirpated the pineal gland in ten chickens, seven of which survived the operation. Five of these were hens. The results of this experiment confirmed the results of the first. He also extir-

pated the pineal gland from eight young rats, four of which survived the operation; three of these were males. No noticeable effect was produced on the female, but the males attained the maximum somatic development more rapidly than the controls.

Christea ('12) extirpated the pineal gland in thirty cockerels, twelve of which survived the operation. The development of the body was not particularly delayed, but the retardation in the secondary sexual characters (comb, spurs, voice) was very marked. The growth of the feathers was retarded and a marked atrophy of the testicles occurred.

Sarteschi ('13) extirpated the pineal gland in twenty-three young rabbits. Two of the three that survived the operation were males. In one of the males, when killed at the age of five months, the testicles were greatly hypertrophied. In the other operated male, killed when nine months old, the testicles were smaller than in the male previously killed. The female was apparently unaffected by the operation. Examination of the brains showed that in all of these operated rabbits a remnant of the pineal gland was not removed. He also extirpated the pineal gland in fifteen puppies, three of which survived the operation. The extirpation of the gland was complete. In all of these the testicles were considerably hypertrophied and one attained a much greater somatic development and a tendency to great obesity. From these results he concluded that the extirpation of the pineal gland results in an accelerated somatic and a precocious and augmented sexual development. In 1910 two young rabbits survived a series of his extirpation experiments. These showed a retardation in growth and cachexia which disappeared.

Adler ('14) destroyed by thermocautery the pineal gland in tadpoles. One hundred of the 850 operated animals survived the operation four days. At the end of twelve days thirty were still alive, and at the end of nineteen days only nine were living. These developed irregularly when compared with the controls. Seven out of the nine developed edema. Three of the edematous animals lived to be eighty-one

days old, while four of these died previously. The two non-edematous animals lived eighty-two days. There was no abnormality in sexual development. None of the operated animals completely metamorphosed. He is of the opinion that the irregular development and incomplete metamorphosis were due to a disturbance in the endocrine system brought on through pinealectomy.

Dandy ('15) removed the pineal gland from young dogs ranging in age from ten days to three weeks and also from full-grown dogs. The results were negative, and he believes that the "pineal gland is apparently not essential to life and seems to have no influence upon the animal's well being."

Horrax ('16) performed a pinealectomy operation on eighty-two guinea-pigs which ranged from two days to seven weeks in age. Forty-eight of these lived to maturity or until sacrificed. These were killed at variable intervals, the oldest being ninety-eight days of age when killed. Microscopic examination showed that the gland was totally removed in fifteen males and twenty females. "Pinealectomized male guinea-pigs show a hastened development of the sexual organs, manifested before maturity by a relative increase in size and weight, both of the testes and seminal vesicles, over control pigs of the same litter." A histological examination of the testes and seminal vesicles in animals before sexual maturity showed a more advanced physiological state than their controls. "The pinealectomized females appear to show a tendency to breed earlier than controls of the same age and weight." He also removed the pineal gland in young rats, but an epidemic almost ruined this experiment. However, the results showed "some evidence of hastened maturity" in the males.

Hoskins and Hoskins ('19) removed the pineal gland from seventy young larvae of *Rana sylvatica*, but it regenerated either partially or completely and the larvae grew normally. The anlage of the pineal gland was also transplanted into young larvae, but it failed to grow.

If one summarizes briefly the above historical sketch, the results obtained by previous investigators from the extirpation of the pineal gland can, in a general way, be placed into four groups: A) a retardation in the development of the genital characters or of somatic growth; B) an acceleration in the development of the genital character or of somatic growth or of both; C) negative results, and, D) regeneration. Into one or two of these groups fall the results of the various investigators, as follows:

A. 1) Retardation in the development of sexual characters—comb, spurs, voice, feathers, and atrophy of the testicles. Cockerels (Christea, '12). 2) Retardation in growth and cachexia which disappeared. Young rabbits (Sarteschi, '10). 3) Irregular growth and incomplete metamorphosis. Tadpoles (Adler, '14).

B. 1) Hastened maturity. Male rats (Horrax, '16). Acceleration of somatic development. Male rats (Foa, '14). 2) Accelerated and augmented development of the sexual organs in male guinea-pigs and a tendency to breed earlier than the controls in female guinea-pigs (Horrax, '16). 3) Acceleration and augmentation of the primary and secondary sexual characters. Cockerels (Foa '12, '14). 4) Accelerated somatic and a precocious and augmented sexual development. Young rabbits (Sarteschi, '13).

C. Negative results. Young rabbits (Exner and Boese, '10). Young dogs (Dandy, '15). Adult dogs (Biedel, '13). Female rabbit (Sarteschi, '13). Female rat (Foa, '15). Hens (Foa, '12, '14).

D. Regeneration followed by normal growth. Tadpoles (Hoskins and Hoskins, '19).

The discrepancies in the results following the extirpation of the pineal gland, as indicated above, warrant a repetition of this method of experimentation.

Single-comb White Leghorn chicks were selected for this work because they reach maturity in less than a year. In 1920-21 an experiment with chicks was carried through, but

on account of a comparatively large number dying of an intestinal disturbance the experiment was repeated in 1922. The experiment of 1920-21 will be designated as experiment no. 1, while the one of 1922, as experiment no. 2. The operated and control cockerels and hens of each experiment were kept together in the same pen and received the same food throughout the duration of the experiment.

It is difficult to distinguish the sex in newly hatched chicks. Generally the larger ones and also those that were apparently the most vigorous were selected for operating.

Precautions necessary for an operation under aseptic conditions were observed. The chicks were anesthetized with ether. The skin was prepared by shaving and by applying iodine-alcohol. A median-line incision of the skin about $1\frac{1}{2}$ cm. in length was made on the crown of the head. With a sharp knife (Gillette razor blade) bone was removed from the region above the pineal gland, care being exercised not to cut the dura. In newly hatched chicks the bones of the calvarium are thin and can be easily cut. An incision was then made in the dura large enough to permit readily the insertion of the points of small forceps with which the pineal gland was removed. It is impossible to avoid cutting the dural sinuses in that region and also injuring the great cerebral vein, so that some mortality resulting from hemorrhage is unavoidable. Immediately after the removal of the gland the wound was swabbed with a solution of lysol, the skin sutured, and an antiseptic applied to the wound. The majority of the chicks recovered rapidly from the effects of the operation, and in one to three hours began to search for food, while a few remained droopy for a longer time.

Thirty-six chicks of experiment no. 1 were removed from the incubator June 1. An operation for the extirpation of the pineal gland was performed on twenty-nine chicks on June 4 and 5. Two died during the operation from an overdose of ether; three died shortly after the operation from hemorrhage. From an intestinal disturbance four died previous to

June 16, two on July 5, one on July 17, and one on August 16. One male was killed by a cat on June 24 and one hen died from a cause unknown to me on October 31. Hence, only six of the operated chicks (four cockerels and two hens) reached maturity. Of the fifteen control chicks six died from an intestinal disturbance previous to June 16. Nine (five cockerels and four hens) reached maturity.

On June 16 both the control and operated chicks were labeled with leg bands and weighed for the first time. Thereafter they were weighed weekly up to November 18, from which date on to the time they were killed they were weighed, with few exceptions, only biweekly.

The chicks of experiment no. 2 were obtained from two hatches which will be referred to as hatch no. 1 and hatch no. 2.

Hatch no. 1 consisted of twenty-four chicks which were removed from the incubator on April 7. A pinealectomy operation was performed on nineteen chicks on April 11 and 12. Two died during and seven shortly after the operation. One control chick died on April 16 and an operated hen that was sick for four continuous weeks was killed on June 13.

Hatch no. 2 consisted of thirty-three chicks which were removed from the incubator on April 11. Nineteen underwent a pinealectomy operation on April 15. Five of these died shortly after the operation. One hen died of roup on August 17. Of the control chickens one cockerel disappeared from the pen August 19. One operated cockerel and one operated hen of hatch no. 1 were killed June 14, and one control cockerel and one control hen of hatch no. 2 were killed June 20.

The chickens that reached maturity of experiment no. 2 (hatches no. 1 and no. 2) consisted of six operated cockerels, thirteen operated hens, four control cockerels, and twelve control hens.

On April 24 the control and operated chicks of both hatches were labeled with leg bands and weighed for the first time. Thereafter they were weighed weekly up to August 7. From

that date to the time they were killed they were weighed, with few exceptions, only biweekly.¹

An examination of serial sections of the brains of the operated chickens that lived to the termination of the experiments showed that in experiment no. 1 the pineal gland was completely removed from three cockerels and two hens and only partially removed from one cockerel, and in experiment no. 2 the gland was completely removed from two cockerels and from four hens and only partially removed from four cockerels and nine hens. The chickens of the two experiments fall, therefore, into six groups as follows: *a*) control cockerels; *b*) control hens; *c*) successfully operated cockerels; *d*) successfully operated hens; *e*) unsuccessfully operated cockerels, and, *f*) unsuccessfully operated hens. The 'successfully operated' cockerels and hens are those in which the extirpation of the pineal gland was complete, while the 'unsuccessfully operated' cockerels and hens are those from which, unintentionally, only a part of the gland was removed.

Table 1 shows the average initial weights of the chickens in each group and the average weights of the chickens in each group at weighings made at intervals (with few exceptions) of four weeks, as indicated by the dates. From the data given in table 1 the growth curves represented in figures 1, 2, 3, and 4 were drawn. The average initial weight of the chicks in each group was used as a starting-point for the curve of that particular group.

The growth curves of the different groups of chickens in experiment no. 1 represent a period of growth of 269 days' duration. After this time the weight of some of the chickens began to fluctuate from one weighing to the other, indicating that full growth had been reached. On account of the fluctuation in weight of a full-grown chicken, the average weights of the cockerels when they were killed (table 2) does not correspond to the average weight represented by the highest point of the growth curve.

¹ The average initial weight of the chicks in hatch no. 1 was slightly greater than that of the chicks in hatch no. 2. This difference between the average weights gradually disappeared toward the termination of the experiment and was not taken into consideration in plotting the growth curves.

TABLE 1
Average weights of the chicks. On June 16th and April 24th the chicks of the two experiments were weighed for the first time

EXPERIMENT NO. 1 CHICKS REMOVED FROM INCUBATOR JUNE 1ST							EXPERIMENT NO. 2 CHICKS REMOVED FROM INCUBATOR APRIL 7TH AND 11TH ¹							
	Age in days	Average weight of three successfully operated cockerels	Weight of one unsuccessfully operated cockerel	Average weight of five control cockerels	Average weight of two successfully operated hens	Average weight of four control hens		Age in days	Average weight of two successfully operated cockerels	Average weight of four unsuccessfully operated cockerels	Average weight of four control cockerels	Average weight of four successfully operated hens	Average weight of nine unsuccessfully operated hens	Average weight of twelve control hens
June 16	16	91.3	98	99.2	101	87.5	April 24	15±2	97.5	92.7	90.2	80.5	76.1	78.7
July 14	44	215.7	242	268.2	238.5	217.5	May 15	36±2	250.5	262.7	227.2	181.7	213.8	191.4
August 11	72	371.7	374	468.8	379	376.2	June 12	64±2	505.5	619.5	573.7	384.5	490.7	416.5
September 8	100	549.3	495	719.4	519	557.2	July 10	92±2	741.5	904.2	826	569.5	689.3	590.6
October 7	129	812.7	550	1064	741.5	771.5	August 7	120±2	720.5	914.5	925	573.5	663.1	621.6
November 4	157	1112.3	871	1323.4	907	949.2	September 4	148±2	960.5	1218.7	1290	782.5	925.7	814.8
December 2	185	1529.7	1252	1636	1169.5	1181.7	October 2	176±2	1189	1383	1445.2	948.2	1092.2	992
December 30	213	1751	1465	1831.6	1452.5	1349.7	October 30	204±2	1414	1651	1615.3	1071.3	1313.4	1077.6
January 27	241	1842.7	1735	1967	1666.5	1524.5	November 13	218±2				1185.	1406.2	1092.4
February 24	269	1899.7	1810	2090.7	1781.5	1582.3	November 23	228±2	1492.5	1755.2	1687.3			

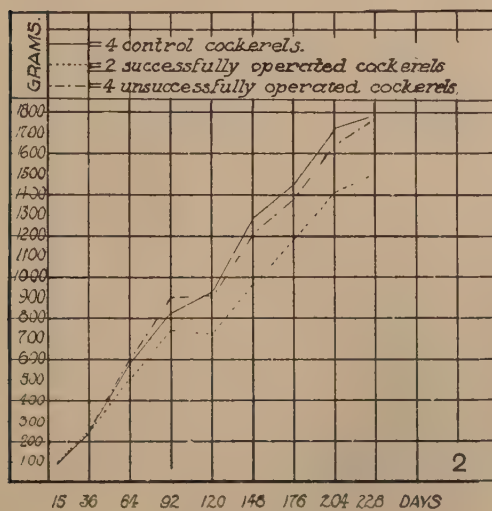
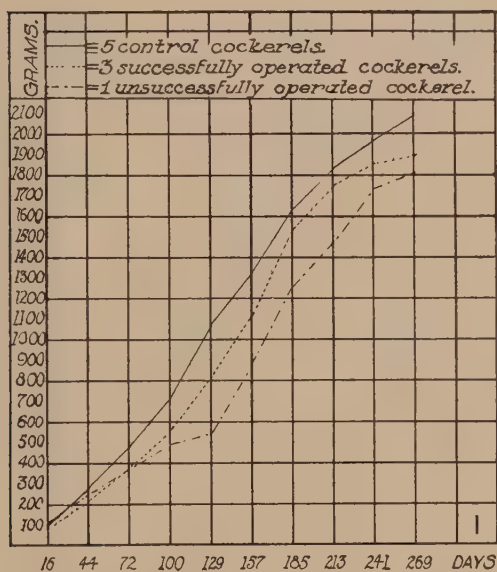
¹ The chicks in hatch no. 1 were four days older than in hatch no. 2. April 9th was, therefore, selected as the date from which to calculate the age. Each group has in it chicks from both hatches. Hence the '±' in connection with the age of the chicks.

Foa ('12) found that the extirpation of the pineal gland in chicks retards the development of the body of the cockerels during the first two or three months following the operation, but has no effect on the hens. Foa used for controls cockerels and hens which underwent a sham operation, i.e., the operation was carried through in the usual manner except that the pineal gland was not removed. The unsuccessfully operated chicks in my experiments furnish, therefore, a type of controls which, to some extent, are similar to those used by him.

If the data of the two experiments as represented by the growth curves are compared, it will be seen that the successfully operated cockerels of both experiments suffered a slight retardation in the average rate of body growth when the comparison is made with the growth of the control cockerels (figs. 1 and 2). The period of retarded growth was greater in duration in experiment no. 2 than in experiment no. 1. If, however, the comparison is made with the average rate of body growth of the unsuccessfully operated cockerels, which are comparable to the controls of Foa, the results of the two experiments differ. In experiment no. 1 the average rate of body growth of the successfully operated cockerels was more rapid (which does not agree with the results of Foa), while in experiment no. 2 less rapid (which agrees with the results of Foa) than the average rate of body growth of the unsuccessfully operated cockerels.

If the comparison is made between the controls and the unsuccessfully operated cockerels, the results again are different for the two experiments. In experiment no. 1 the average rate of body growth was greater for the controls than for the unsuccessfully operated cockerels, while in experiment no. 2 the average rate of body growth was about equal for these two groups of cockerels.

A quite uniform average rate of body growth is manifested for the control and successfully operated hens in both experiments (figs. 3 and 4). If a comparison is made between the unsuccessfully operated hens (which are comparable to the control hens of Foa) and the successfully operated hens in



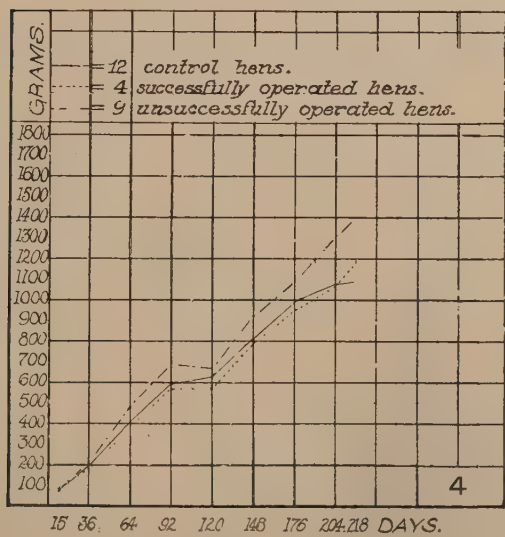
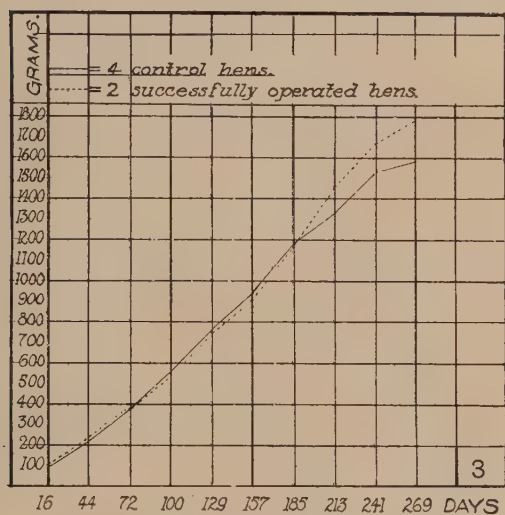
Figures 1 and 2

experiment no. 2 (fig. 4), it will be seen that the average rate of body growth of the latter was less, during the greater part of the experiment, than for the former. This result again does not agree with the conclusion of Foa, who claims negative results following the extirpation of the pineal gland from hens.

Foa claims that after the period of retarded growth the operated cockerels attain the body weight of the normal adults. This conclusion is confirmed by the results in experiment no. 1, which was of a sufficient duration for the cockerels to attain their full growth. Experiment no. 2 was about seven and one-half months in duration. The cockerels were sexually mature, but were not fully grown and at the termination of the experiment the average weight of the successfully operated cockerels was less than that of the cockerels in either of the other two groups.²

From the above considerations it is very evident that discrepancies in the results between experiments nos. 1 and 2 and also between these two experiments and those of Foa are manifest. The factors that were perhaps most responsible in confusing these results are the great variations in the rate of growth of chickens and the small and variable numbers of them used in each group for comparisons. The latter factor particularly augmented the chance for inaccuracy. From the data represented by the growth curves in figures 1 and 2, I cannot see that one is justified in drawing the conclusion of Foa of a period of retarded growth of the cockerels due to pineal deficiency, for the rate of body growth of the successfully operated cockerels when compared with the rate of body growth of the unsuccessfully operated cockerels (comparable to Foa's controls) do not agree in the two experiments. It is also improbable that the vitiating effects of the operation

² The very slight gains in weight made by some of the groups of chicks and the actual loss suffered by other groups from the ninety-second to the one-hundred-and-twentieth days in experiment no. 2 (figs. 3 and 4) were undoubtedly due to weather conditions. During this period the weather was unusually hot and dry. The successfully and unsuccessfully operated cockerels and hens were apparently more adversely affected than the control cockerels and hens.



Figures 3 and 4

affected the body growth of the chicks for any considerable length of time, for the average rates of body growth are about the same for the control and unsuccessfully operated cockerels in experiment no. 2 (fig. 2), and the controls and successfully operated hens in experiments 1 and 2 (figs. 3 and 4), while the average rate of body growth of the unsuccessfully operated hens was even greater than for the controls (fig. 4). From the results of these experiments I am inclined to believe that the seemingly retarded rate of body growth of the successfully operated cockerels in both experiments, when compared with the rate of body growth of the controls, is a mere coincidence and not brought about by any physiological disturbance due to pineal-gland deficiency.

In experiment no. 1 the total of the average weights of the right and left testicles is greater by 15 per cent for the successfully operated cockerels than for the control cockerels and greater by 8.6 per cent than for the unsuccessfully operated cockerel. Foa maintains that a precocious and exaggerated development of the primary and secondary sexual characters are a consequence of apinealism. In his experiment ('12) he compared the 'weight of a testicle' of an operated cockerel with the 'weight of a testicle' of a control cockerel. The data on the weights of the testicles as given by him are as follows: No. 1, operated 22 grams, control 13 grams; no. 2 operated 18 grams, control 11 grams, and no. 3, operated 20 grams, control 15 grams. The total testicular weight of the operated cockerels as represented by him is 53.8 per cent greater than the total testicular weight of the controls. In his experiment the weight of the lightest testicle of an operated cockerel was greater than the weight of the heaviest testicle of the control cockerels. In experiment no. 1 (table 2) the heaviest total testicular weight (right and left testicles) was found in control cockerel no. 82, while the total testicular weight of the unsuccessfully operated cockerel (no. 81) was heavier than the total testicular weight of no. 80 and almost equal in weight to no. 84 of the successfully operated cockerels. From the above consideration it is very doubtful that the increment of

15 per cent in the weight of the testicles can be attributed to a lack of pineal-gland secretion, since it falls within the limits of normal variation. In consideration of the great variation in the weights of the testicles, I believe that the number of cockerels used in experiment no. 1 and also in Foa's experiments was much too small to justify drawing any definite conclusions.

The cockerels in experiment no. 2 (table 2) had not reached full growth, although they were (excepting one) sexually mature. The average testicular weight of the successfully operated cockerels is slightly greater than for the control cockerels, but slightly less than for the unsuccessfully operated cockerels. If cockerel no. 16³ is omitted from the group of controls, the average testicular weight of the remaining cockerels of that group is 13 grams, which is greater than the average testicular weight of the cockerels in either of the other two groups. In this experiment there is no indication of an accelerated growth of the testicles of the pinealectomized cockerels, although they were killed at an age when one would expect this feature to manifest itself if it occurs at all.⁴

Foa found that the comb of a fully grown pinealectomized cockerel was much larger than the comb of a fully grown control. His observations indicate that the acceleration of the growth of the comb began in the operated cockerels when

³ Cockerel no. 16 was first recorded as a hen. The male secondary sex characters manifested in plumage and comb developed slowly and never became as pronounced as in the other cockerels of this group. It seldom crowed and was never seen to tread hens. It weighed the least of any of the control cockerels. Throughout the entire experiment it retained somewhat 'henney' features. On account of this apparent abnormality, it appears justifiable to omit the weight of its testicles.

⁴ The left testicle of a fully grown cockerel is generally larger than the right one (table 2, expt. 1). An interesting feature brought out by experiment no. 2 is that the right testicle was larger than the left one in the majority of the cockerels when killed at the age of about seven and one-half months, or about one and one-half to two months before they are fully grown. Apparently at about this age the 'growth impulse' is generally greater for the left than for the right testicle, resulting in a larger left than right testicle in a fully grown cockerel.

they were about six months old. The data in table 2, experiment no. 2, do not indicate an accelerated comb growth of the successfully operated cockerels, even though they were killed at an age when, according to Foa, this feature should have manifested itself.

The record that was kept of the combs of the cockerels in experiment no. 1 was, unfortunately, only in the form of notes. The combs were not weighed, hence the record is of little value. The record showed a great variation in the size and a slight variation in the number of notches of the combs of the cockerels in all groups, but not anything unusual to attract particular attention to the combs of the successfully operated cockerels.

Foa observed that the operated cockerels manifested the sexual instinct (copulation) from forty-two to seventy-nine days sooner than the control cockerels. In observing particularly the primary and secondary sexual characters (sexual instinct, crowing, comb) of the chickens in experiment no. 2, I found it difficult to determine the exact age at which fruitful copulation first took place. Both operated and control cockerels attempted treading hens before either they or the hens were sexually mature. As far as could be observed, sexually immature hens invariably resent the treading of the cockerels. Some cockerels attempt to tread hens when considerably younger than others and some much more frequently than others. Apparently, individual characteristics vary considerably in this respect. My observations do not confirm a precocious development of the sexual instinct of the pinealectomized cockerels.

The majority of the cockerels, both operated and controls, began to crow during the first three weeks in June. One unsuccessfully operated cockerel (no. 6) made an attempt at crowing May 28 and another (no. 35) of the same group on May 29. Some cockerels learn to crow well in less time than others and some crow more often than others. Cockerels nos. 29, 30, 33, 35, and 42, which include cockerels of every group, were great crows. These observations do not agree with the

TABLE 2
Weights and average weights in grams of cockerels, testicles and combs

Experiment no. 1	Experiment no. 2
Successfully operated cockerels	Successfully operated cockerels
Unsuccessfully operated cockerels	Unsuccessfully operated cockerels
Control cockerels	Control cockerels
Label number of cockerel	Label number of cockerel
Date when killed	Date when killed
Age in days when killed	Age in days when killed
Weight when killed	Weight when killed
Average weight when killed	Average weight when killed
Weight of right testicle	Weight of right testicle
Weight of left testicle	Weight of left testicle
Average weight of right testicle	Average weight of right testicle
Average weight of left testicle	Average weight of left testicle
Total of the average weights of testicles	Total of the average weights of testicles
Weight of combs	Weight of combs
Average weight of combs	Average weight of combs

conclusion of Foa that the pinealectomized cockerels crow sooner than the controls.

As previously stated, an operated and a control cockerel of experiment no. 2 were killed on June 14 and 20, respectively. The operated cockerel was sixty-eight days old and weighed 682 grams, while the control was seventy days old and weighed 536 grams. These were selected because the operated cockerel had, at that time, the largest, and the control cockerel next to the largest comb of any of the cockerels in the flock, and both were very energetic, crowed lustily often, and made frequent attempts at treading hens. These cockerels were killed at this time in order to determine approximately the age at which the acceleration in the growth of the testes of pinealectomized cockerels begun, if such was the case. The total testicular weight of the operated cockerel was 3.7 grams, while that of the control 2.2 grams. A microscopical examination showed the presence of spermatozoa in the testes of both cockerels. However, a microscopic examination showed that the pineal gland in the operated cockerel was not all removed, thus nullifying the attempt at this phase of the experiment. It, however, did show that at this age the primary and secondary sexual characters were not manifest to as great a degree in the pinealectomized cockerels as in some of the control and unsuccessfully operated cockerels.

Of the hens in experiment no. 2, the first egg was laid by a control September 24. An unsuccessfully operated hen laid its first egg September 27, and another of the same group on October 9. From about the middle of October it was difficult to make accurate observations on the laying of eggs. More hens began to lay and also some did not lay the eggs in the nests prepared for them. It was, however, definitely observed that the pinealectomized hens were not the first to lay eggs, thus confirming the negative results obtained by Foa from his operated hens.

The results of my experiments can all be interpreted as negative. These agree with the results obtained by Foa from pinealectomized hens, but not with the results obtained by

him from pinealectomized cockerels in which an acceleration and augmentation of the primary and secondary sexual characters were manifested. Neither do the results of my experiments agree with those of Christea, who claims for the pinealectomized cockerels a retardation in the development of the genital characters—comb, spurs, voice, feathers, and atrophy of the testicles.

When the variable results of pinealectomy operations on animals of the same and different species are compared, it is evident that a condition, whatever it may be, exists that prevents the interpretation of these experiments.

The feeding of pineal substance from young animals to young animals seems to have yielded more uniform results. Dana and Berkeley ('13) fed pineal-gland extract to young guinea-pigs, rabbits, and kittens. They are of the opinion that the nutrition of the body was influenced, manifested by a general growth, development of the genital organs, and a deposit of subcutaneous fat, above the normal. Berkeley⁵ in 1920 again repeated these feeding experiments, which resulted in an acceleration of the somatic growth to a marked degree.

McCord ('14, '15) fed pineal-gland extract to chicks, guinea-pigs, and puppies, and also administered the extract by injection to guinea-pigs. The results were a more rapid growth of the body than normal and an early sexual maturity. "Both males and females respond to the influence of pineal substance in rate of growth, but the response has been more definitely manifested in males."

The results of these feeding experiments are contradictory to the now-prevailing notion of the function of the pineal gland. Precocious development, which is generally attributed to pineal-gland deficiency, was induced by supplying an excess of pineal substance by feeding. The majority of extirpation experiments which yielded decided positive results also gave more or less definite pictures of a precocious development. As far as I was able to determine, the extirpation experiment of Christea is the only one that gave definite results which

⁵ Cited by Krabbe ('23).

seem to be consonant with those of the feeding experiments of Dana and Berkeley and of McCord.

When one reviews the literature of the work that has been done on the pineal gland (extirpation, feeding, injection, transplantation, stimulation, embryology, clinical, and pathological studies), one is forced to take the view that, at the present time, our knowledge of this organ is too meager to draw any definite conclusions concerning its function. In my experiments the extirpation of the pineal gland apparently did not disturb the well-being of the chickens.

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RAT CAGES OF SIMPLIFIED CONSTRUCTION

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TEN FIGURES

In the maintenance of colonies of small mammals there is need of compactly arranged cages of simple construction and reasonable cost. The type described below is the outcome of several years' experience, and having been found satisfactory here may be of use to others.

The cages are of sheet metal and are supported on a rack made of wood and iron pipe. The general appearance of such a rack of cages is shown in figure 1; more detailed views in figures 2 and 3, and plans of the several parts in figures 4 to 10.

The rack consists of two wooden frames (figs. 1 and 10) and several pairs of iron pipe (nine pairs in the rack shown in fig. 1) of 1 inch outside diameter, which are inserted into the frames at right angles to them and at exact intervals. It is to be noted that the dimensions given in figure 10 should be followed exactly, otherwise the metal cages will not fit properly into the rack. The size of the rack (number of rows of cages and number of cages to the row) may be varied to suit individual needs.

The cages are made in four parts: 1) top and bottom, with lid or door attached, 2) side or vertical partition, 3) back, 4) tray. The 'top and bottom,' as the name implies, serves for the top of one cage and the bottom of the one immediately above it. It is made of two pieces of metal, a larger and a smaller. The larger of the size and shape shown in figure 4 is cut from sheet metal and bent along the dot-and-dash

lines (fig. 4) into the form in figure 5. To its under side the smaller piece (to which the lid is hinged by simple rings) is riveted and soldered in the position shown in figure 5. It will be observed (figs. 5, 6, 2 and 3) that the side flanges of the 'top and bottom' rest on a pair of pipes, supporting the bottom $\frac{1}{4}$ inch above the pipes. In assembling the cages the



Fig. 1 Front view of a rack of forty-eight cages.

rear end is placed on the rear pipe first, and when the front is in place and the front flange clasps the front pipe, because of its curved form, the rear end of the bottom cannot



Figure 2

Figs. 2 and 3 Front views of cages to show some details of construction and the device for locking the lids. Notice that the projecting of the trays beyond the floors makes it easy to grasp the end of the tray.

be raised by reason of the oblique cut in the side flanges (figs. 5 and 6). Between the rear flange and the rear pipe is a space of $\frac{1}{4}$ inch to receive the upper end of the back. While the bottom is raised $\frac{1}{4}$ inch above the pipes by the side flanges, the side flanges themselves extend $\frac{3}{4}$ inch below the pipes. When two bottoms are side by side and two tops are placed



Figure 3

on the next pipes above, a partition may be slipped in between, resting on one pair of pipes and being supported laterally at top and bottom by the flanges (figs. 2 to 6).

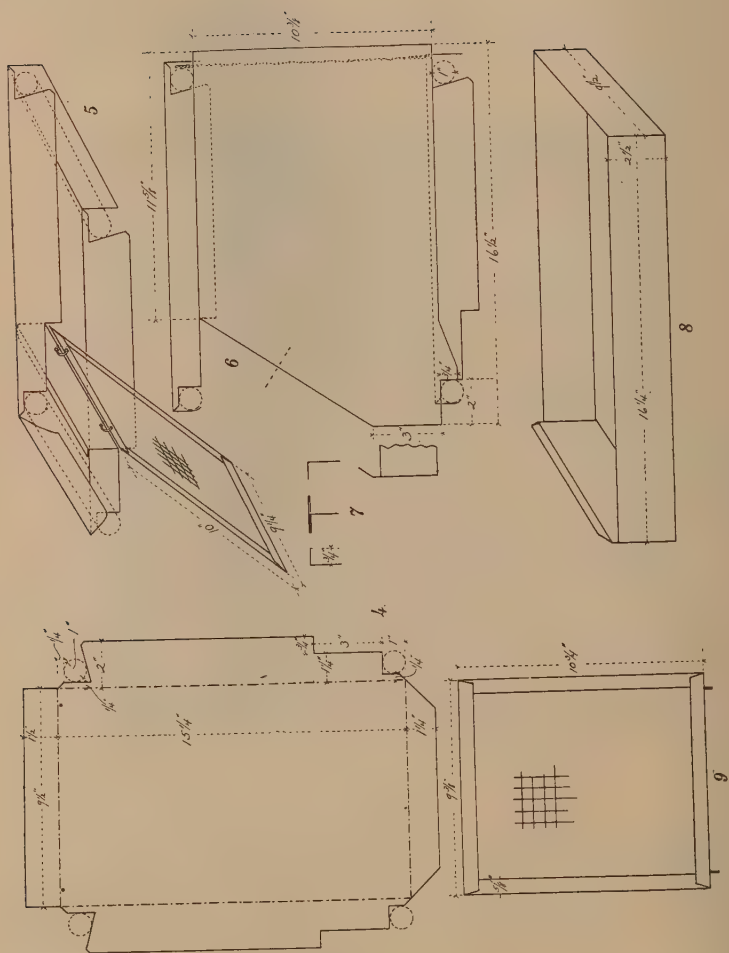
The sides or vertical partitions are of the simplest possible construction, being cut from sheet iron in the form shown in figure 6. All edges are plain except the front oblique edge, which is flanged. The flanges on the partitions at the ends of a row are formed by bending the metal to one side or the other

at right angles (fig. 7). On the other sides or partitions the flange is double (middle fig. 7; also figs. 2 and 3). The upper end of the flange rests against the offset in the side flange of the top (figs. 6 and 2), and thus prevents the partition from slipping back too far. The lug on its lower edge resting against the rear side of the front pipe keeps the partition from being pulled forward when the trays are removed.

The lid (fig. 5) is a piece of $\frac{3}{8}$ -inch-mesh wire cloth bound with strips of sheet iron. The back (fig. 9) has a similar construction. In addition on the lower edge of the back are two pins which fit into two holes in the floor close to the rear edge. The back is put into position by slipping its upper end upward between the rear pipe and the rear flange of the tops and then dropping it so that the pins fit into the holes. The backs also give lateral support to the sides or partitions. The bottoms of the lower row need no lids.

The tray should be made to fit snugly against both the sides and the back when it is pushed into position so that the oblique, flange-like part of the front just overlaps the lower ends of the flanges on the sloping front edges of the sides.

It will be seen that the parts are very simple, easily made, and therefore relatively inexpensive. The cages can be taken down and cleaned, although that is not often necessary, for the animals cannot climb about on the under surface of the roof and are effectively kept off the floor by the tray except when that is withdrawn for changing the shavings, or sawdust. Neither can the animals climb on the sides, the back and lid being chiefly used for gymnastics. Plenty of air has access from front and back through the $\frac{3}{8}$ -inch-mesh wire cloth. There is no waste space between rows and no crevices into which escaped wild animals can creep; consequently, a large colony can be housed in a small space. If larger cages are desired, as many sides or partitions can be left out as need be, two or more trays being in contact. The lids are so close together that animals cannot escape through the cracks between them. Or openings can be made in the partitions large enough to allow animals to pass from cage to cage—an ar-



Figures 4 to 9

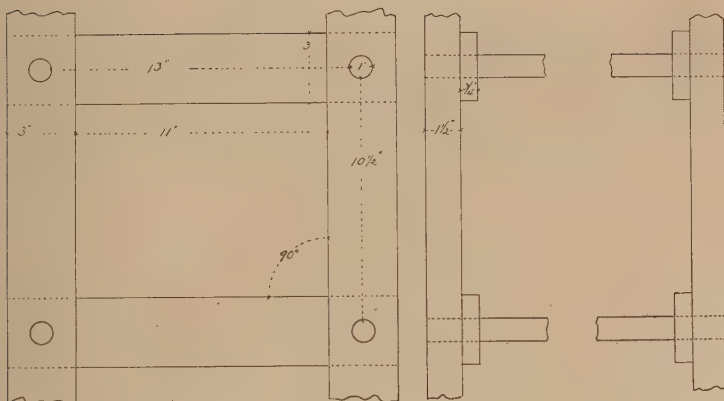


Figure 10

Fig. 4 Pattern for cutting sheet metal for the top and bottom. The flanges are all bent at right angles to the same side along the dot-and-dash lines, as shown in figure 5.

Fig. 5 A top and bottom consisting of two pieces; to the under side of the larger (fig. 4) is attached the smaller, to which in turn is hinged the lid or door.

Fig. 6 Pattern of a side or partition shown in place between two pairs of pipes; also side views of two tops and bottoms (without the lids) in place on the same pipes and in proper relation to the side. Notice the position of the back. The pins are not shown in the figure, but can be seen in figure 9 and also in figure 3 just above and to the right of the cage number '125.' The front end of the tray is represented as partly withdrawn to show how the oblique portion of its front end corresponds to the slope of the oblique edge of the side. In cutting the pattern for the side, metal must be left along the oblique edge for the flange (fig. 7).

Fig. 7 Sections along the dotted line on the oblique edge of the side (fig. 6). At the right and left are shown the simple flanges for the partitions or sides at the ends of the rows of cages; in the middle the double flange for all other partitions.

Fig. 8 The tray.

Fig. 9 The back.

Fig. 10 Details of the construction of the rack which consists of two ladder-like wooden frames and iron pipe.

rangement advantageous in the case of wild animals which can be chased into one cage while the adjacent one is being cleaned.

Another useful feature is the lock for the doors or lids. This is shown in figures 1 and 3. A whole row is locked by merely turning down the stick, which is swung on two short pieces attached to the inner sides of the end frames and secured in position by the wooden buttons also on the frames.

A CASE OF CYCLOPIA IN HOMO

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EIGHT FIGURES

INTRODUCTION

The late Professor Mall, in his paper entitled "Cyclopia in the human embryo" ('17), calls attention to the rarity of anatomical data in the literature on that type of abnormality. "And it may be remarked," he adds, "that until we have numerous good descriptions (like that of Black) of the eyes, central nerves, and face in cyclopia, we shall not understand fully the anatomy of this most interesting type of specimen."

The cyclopean condition is of course somewhat rare in man, and to this rarity we may in part ascribe the limited number of anatomical studies upon human material. The desire to preserve specimens intact for museum purposes still further reduces the number available for dissection. As a result, but few human cyclops have been described except as to external features. In lower vertebrates, in which cyclopia can be produced at will through chemical or mechanical treatment (Stockard, '09; Lewis, '09), it would seem we should have unlimited material for study of its anatomical features. Yet even here, in the majority of cases, the reports deal chiefly with the external features of the malformation.

The cyclopean fetus described in the following pages was received preserved in strong formalin. Though the fixation of the brain was so poor that a study of its tracts and their

¹ The case of cyclopia here described was made available for study through the kindness of Dr. A. T. Kerr, of Cornell University Medical College, in whose laboratory the dissection was performed.

connections was impossible, the eye and other structures of the orbit were found to be in an excellent state of preservation.

DESCRIPTION OF THE CASE

A. External features in general

The specimen, a well-developed male infant at term, weighs 2355 grams (5.2 pounds). The body is to all appearances normal in development, as are likewise the lower portions of the head and face. Due to a great reduction in the size of the cerebral portion of the cranium, the head is somewhat microcephalic in type. Measured over the fleshy structures, its greatest transverse diameter is 7.5 cm., while its greatest length is 8.5 cm.; the cephalic index is 88.2. The marked reduction in size of the skull toward its apex is well illustrated in figures 5 and 6.

The single large eye (fig. 6) is situated medially, but a short distance below the hairy portion of the scalp. The low forehead bears no traces of the nose such as are so frequently encountered in this situation in cyclopia, while between the orbit and the mouth only a shallow depression is evident. The palate shows no indication of the cleft condition and the upper lip is perfectly formed.

B. External features of the eye

The eyeball protrudes from the orbital fossa as indicated in figure 5. It is nearly circular in outline. The exposed surface is of a dark brown color throughout, except for two distinct light areas laterally placed—the pupils. Related to each pupil is a cornea rather poorly distinguishable from the surrounding sclera. The uveal pigmentation is doubtless responsible in part for the deep color of the bulbus. Pigment, however, is to be found in the cornea and sclera as well; the conjunctiva and even the edges of the lids are likewise deeply colored—a condition not usually encountered in the normal eye. Sections show this pigment to be in the connective tissue or in apparently occluded blood vessels.

The superior palpebrae (fig. 7) are united to form a single lid, beset with cilia throughout, and marked along its free edge with alternating light and dark bands. Lacrimal papillae are absent. Near the lateral canthi the conjunctival sac extends backward for some distance before it terminates at the superior fornix. This distance decreases toward the midline, where the conjunctiva is reflected directly from the anterior bulbar surface to the edge of the lid.

The inferior palpebrae begin at the lateral canthi and extend medially and downward, each forming with the midline an angle of about 45° . Their ciliated portions terminate, about 9 mm. from the lateral canthi, in well-defined lacrimal papillae, on which the usual punctae are easily seen with the aid of a hand lens. Between the lacrimal papillae and the midline, each inferior palpebra has the usual rounded margin, quite free from cilia. Like the superior palpebrae, the inferior are deeply pigmented and meet at the midline. Lying immediately above their junction is a stout T-shaped structure representing the united carunculae of the two sides. This is separated from the eyeball by a low conjunctival fold, continuous on either side with a lid-like structure—the plica semilunaris. The plica of the right side is particularly well developed; that of the left is more closely adherent to the sclera. Both plicae are unusually large in comparison with those of the normal eye, extending practically to the lateral canthus of either side. Their development approximates that of the nictitating membranes seen in the eye of a cat or dog. Sections, however, show that no cartilage is present, but that the free edge of the fold is made up of a very dense connective tissue, with pyknotic nuclei and areas of complete hyaline degeneration.

The conjunctival sacs of the two sides are deepest laterally. Below the bulbus they are separated medially by the fused carunculae, and, superior to this structure, by the low fold joining the plicae across the midline.

Above the orbit the supercilia are present as two hairy ridges, distinct laterally, but not well marked for about 1 cm.

across the midline. They are separated from the superior palpebrae by shallow grooves—the superior orbitopalpebral sulci. At the inferolateral margin of the eye on either side are two other grooves representing the inferior orbitopalpebral and the infrapalpebral sulci. These, as shown in figure 7, have the usual relations to the eye, their changed inclination, of course, being in accord with that of the inferior palpebrae to which they are related.

C. Cranial cavity and basis cranii interna

Preliminary to the dissection of the eye, the cranial cavity was exposed by removal of the calvaria. The cavity is greatly reduced in size, its capacity approximating only one-third that of the normal infant at birth.

The falx cerebri and its sagittal sinuses are absent. The tentorium cerebelli, normally occupying a position approaching the horizontal, is here more nearly vertical (fig. 1). Its attached border is related to the parietal rather than the occipital bone. It divides the cranial cavity into two chambers, of which the posterior is somewhat the larger. Its floor, the posterior fossa, slopes rather steeply, but in other respects shows no departure from the normal.

The middle and anterior fossae are not sharply separated as in the normal skull, only a slight rounded elevation suggesting a boundary between them. The hypophyseal fossa is of normal size; it contained a well-developed hypophysis, which when sectioned was found to consist of the usual neural and buccal divisions. Anterior to it a rounded foramen, medial in position, leads forward into the orbit.

Figure 1 shows in diagrammatic fashion the appearance of the combined middle and anterior fossae, after removal of the dura back to the edge of the tentorium. The frontal bone forming the roof of the orbit is lacking over a small area in the midline; there is, however, no suggestion of the presence of an ethmoid element. The posterior part of the orbital roof is formed by the sphenoid, which is here largely membranous and cartilaginous. The foramina of the third,

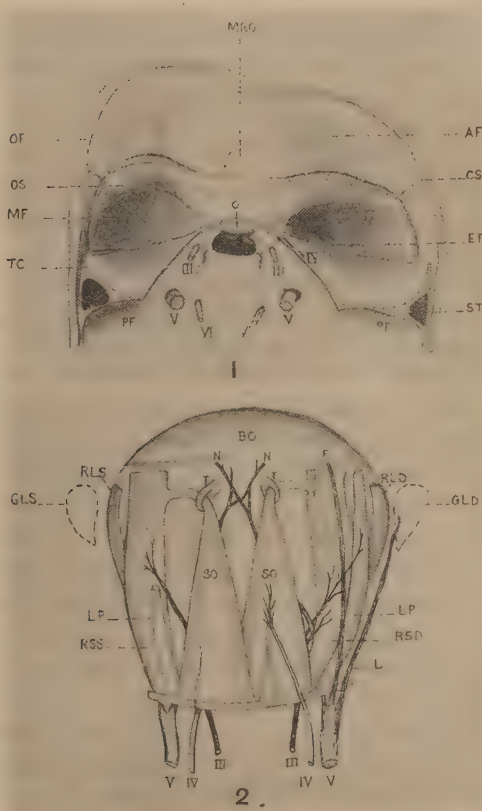


Fig. 1 Basis cranii interni—anterior portion. The dura is represented as removed back to the attached edge of the tentorium cerebelli. The cranial nerves are indicated by Roman numerals. *AF*, anterior fossa; *CS*, coronal suture; *ET*, attached edge of tentorium (cut edge of dura); *MF*, middle fossa; *MRO*, membranous portion of orbital roof; *O*, optic foramen; *OF*, os frontale; *OS*, os sphenoidale; *PF*, posterior fossa; *S*, hypophyseal fossa; *ST*, sinus transversus.

Fig. 2 Muscles and nerves of the orbit as seen from above. Diagrammatic. The nerves are indicated by Roman numerals. The third is shown in solid black; the fourth is unshaded; the fifth is hatched. Branches of the fifth: *F*, frontal; *L*, lacrimal; *N*, nasociliary. *BO*, bulbus oculi; *GLS*, glandula lacrimalis sinister; *LP*, levator palpebrae; *RLD*, rectus lateralis dexter; *RLS*, rectus lateralis sinister; *RSD*, rectus superioris dexter; *RSS*, rectus superioris sinister; *SO*, superior oblique; *T*, trochlea.

fourth, and sixth cranial nerves are not unusual as to situation, and the courses taken by these nerves, before reaching the orbit, are likewise without striking departures from the normal.

D. The brain

The preservation of the brain was such as to make careful histological study impossible. Certain external features, however, may be noted. The cerebellum is well developed. Cerebral hemispheres, on the other hand, are lacking. In their place is a small, somewhat flattened, undivided vesicle, with none of the characteristic convolutions of the cerebral cortex (fig. 8). Along its posterior border, on the ventral surface, is an elevated, crescent-shaped band, narrowest over the midline, which it crosses just anterior to the optic nerve. The lateral portions of this band are expanded and lie flattened between the vesicle and the floor of the middle fossa. That of the right side is closely adherent to the vesicle, while the left ends freely. From its position and nature this structure suggests itself as being made up of the olfactory tracts united medially, the terminal olfactory bulbi, not united, forming the lateral expanded ends shown in figure 8. Sections of the structure fail to show the characteristic olfactory glomeruli. It consists of neuroglia cells and fibers, cells possibly small neurones, and connective tissue. Though the absence of features characteristic of the olfactory lobes does not preclude the possibility suggested above (since the failure of the axons from the olfactory cells to grow into the olfactory bulb may profoundly modify the course of its development), it should, nevertheless, be noted that olfactory lobes, as a rule, have not been found in human cyclopians (Black, '13; Mall, '17).

All other cranial nerves are present (fig. 8). The optic nerves form a single trunk leaving the brain between the hypophysis and the supposed olfactory tracts above described.

The arterial supply of the brain offers no striking abnormalities. Two internal carotids are present; though possibly

smaller than the normal, such a condition would be but a natural result of the absence of cerebral hemispheres. The vertebral arteries unite to form the usual basilar. No posterior communicating arteries were demonstrated.

E. Structure of the orbit

The superior structures of the orbit were first exposed by removal of its bony roof. The side walls were then cut away sufficiently to allow exploration to the level of the lateral canthus.

1. *The ophthalmic nerve.* The ophthalmic branch of the fifth nerve passes forward to the superior orbital fissure. There, on the right side it divides to form three nerves (fig. 2). The most lateral of these is the lacrimal, terminating in a well-developed lacrimal gland situated just above the lateral canthus. The frontal branch passes forward superficial to the other orbital structures, to leave the orbit at its anterior superior margin. The third branch, from its relations, is clearly the nasociliary. It enters the orbit deep to the upper attachment of the lateral rectus and passes forward beneath the superior rectus and superior oblique muscles.

On the left side only the nasociliary division of the ophthalmic can be traced beyond the orbital fissure, a fibrous cord running into the origin of the lateral rectus muscle probably representing the other two divisions. The course of the left nasociliary is similar to that of the right. The two nerves anastomose in symmetrical fashion in the anterior part of the orbit (fig. 2), after which they pass beneath the supra-orbital margin of the frontal bone, to end in the connective tissue and skin above the eye—the situation occupied by a nose in those cyclopians in which that structure is not completely suppressed. Ciliary ganglia were not identified.

2. *Superior oblique muscles.* The trochlear nerves pass through the superior orbital fissures to terminate in large superior oblique muscles, which form the most superficial muscular stratum of the orbit. Though fused at their origin, these muscles diverge as they pass forward. Each forms a

slender tendon, which passes through the usual trochlea, here attached to the roof of the orbit. (The trochleae are situated about 2 mm. from the midline.) The tendons extend laterally; instead of inserting upon the bulbus after passing beneath the superior rectus, each tendon ends by joining the latter muscle near its insertion, as illustrated in figure 2.

At its origin the muscle on the right is divided into two heads (fig. 2). The fourth nerve enters the muscle on its superior surface near the junction of these heads and sends branches into both. No branches of the third nerve can be traced into the muscle—a point of significance in connection with the identification of a medial rectus. The fourth nerve on the left side enters the muscle (superior oblique) on its inferior surface, save for a single small branch; this muscle, like the right, receives no branches from the third nerve.

3. *Levator palpebrae superioris, and medial, superior, and lateral recti muscles.* Lying lateral to the superior oblique of the right side and somewhat beneath it posteriorly are two well-defined muscles taking origin from the superolateral margin of the optic foramen. The smaller and more superficial muscle is the levator palpebrae superioris, since it inserts into the superior tarsus and the conjunctiva. The medial and larger muscle is doubtless the superior rectus. It inserts on the bulbus at a point half-way between the midline and the lateral canthus; its insertion, therefore, has been shifted down through an arc of about 45° . The superior oblique muscle joins the superior rectus at its insertion after the manner shown in figure 2.

The innervation of the right superior rectus is by two branches of the third nerve. The first of these passes superior to the nasociliary nerve to enter the medial surface of the muscle; it thus has the usual relations of the superior division of the oculomotor trunk. The second branch lies below the nasociliary. It sends several branches into the superior rectus, after which it runs forward and laterally to end in the levator palpebrae superioris.

The corresponding muscles of the left side are readily identified. The levator palpebrae superioris is very weakly developed. No nerves to it could be found. The left superior rectus is a large muscle inserting just above the level of the lateral canthus. It is innervated by a single large branch from the third nerve.

The lateral recti have the usual origin and innervation. They insert on the bulbus on either side, at the level of the lateral canthus or slightly below it. Near its insertion each muscle is joined by a flat sheet of muscle from the inferior muscle mass; this will be referred to in detail subsequently. Each lateral rectus has the usual check ligament attaching to the margin of the orbit.

4. *The inferior recti and oblique muscles.* The conjunctiva was cut along the inferior fornix, the cuts of the two sides meeting above the fused carunculae. The eyeball and its muscles were then found to have no attachment to the floor of the orbit, other than by loose connective tissue; the orbital contents were therefore turned backward and dissected from their inferior surface.

The inferior recti are fused into a single muscle, peculiar chiefly in its mode of origin. It arises by seven heads, indicated in figure 3 as follows:

a. A slender tendon from the inferior margin of the left superior rectus.

b. A second and smaller tendon, inferior to *a*, attaching to the superior common tendon.

c. A large tendon from the inferior margin of the left lateral rectus, near its origin.

d. A small fleshy medial head from the inferior common tendon; this narrows to a thread-like tendon lying superficial to *c*.

e. Small left and large right heads, arising medially, deep to the origins of the lateral recti.

f. A slender tendon from the inferomedial surface of the right lateral rectus.

The fleshy portions of the muscle, to which these tendons give attachment, unite in a flattened mass in the anterior portion of the orbit. The fibers from *a*, *b*, *d*, and *f* enter this mass on its deep surface; those of *e* are more superficial; those of *c* extend obliquely across the mass to join its right margin superficially.

The attachments of this inferior muscle mass in the anterior portion of the orbit are five in number. In contrast with the attachment of its tendons of origin, these display a marked symmetry of arrangement. A single strong median tendon (*g*, fig. 3) inserts at the antero-inferior margin of the bulbus. Laterally two narrow bands extend upward from the central mass to attach by flat tendons to the anterior margin of the bony orbit at the level of the lateral canthus (*h* and *h'*, fig. 3). Deep to these bands are two others, shorter and broader (*j* and *j'*, fig. 3) extending from the deep bulbar surface of the central mass to attach to the inferior margin of either lateral rectus. Fibers from each of these deeper bands appear to pass across through the central mass into the superficial band (*h*, *h'*) of the opposite side.

The muscle mass above described doubtless represents incompletely separated inferior recti and obliqui muscles. The attachment of the parts *h* and *h'* to the orbital wall, and the apparent continuation of these into the bands *j* and *j'* inserting on the edges of the lateral rectus suggest that these four structures taken together represent the two inferior oblique muscles, incompletely separated medially from the inferior recti. The single median tendon of insertion would then represent the anterior attachments of the united inferior recti.

The innervation of the inferior muscles is derived entirely from the inferior divisions of the third nerves. These, as indicated in figure 3, anastomose across the median line. Branches running anteriorly from the two nerves likewise anastomose. A branch was followed into the inferior oblique (?) attaching to the left lateral rectus. Small branches on this side appear to terminate in the orbital fat anterior to this muscle. No nerves were traced to the supposed inferior oblique of the right side.

5. *The optic nerve and bulbus oculi.* Extending anteriorly from the optic foramen to the bulbus is a pear-shaped sac formed from the dura (fig. 4). This sac in its largest part approaches the diameter of the bulbus, from which it is marked off by a deep constriction as well as by differences of structure. Inside this dural sac is a second, coextensive with it. The two sacs are readily separated, being attached only

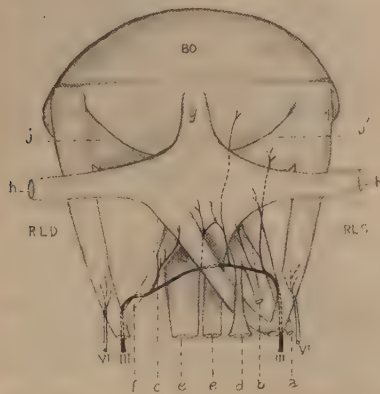


Fig. 3 Inferior orbital muscles as seen from below. Diagrammatic. Third nerve shown in solid black, the sixth unshaded. BO, bulbus oculi; *a*, *b*, *c*, *d*, *e*, and *f*, attachments of origin of the inferior muscle mass (inferior recti); *g*, insertion of same on bulbus; *h* and *h'*, bands of muscle attaching to anterior margin of bony orbit; *j* and *j'*, muscular bands attaching to inferior margins of lateral recti. (*hj'* and *h'j* each probably represents an inferior oblique, the two muscles being incompletely separated from the inferior muscle mass.)

by delicate arachnoidal tissue. The single optic nerve runs along the lower surface of the inner sac, from which it is readily detachable posteriorly (fig. 4, C). Near the bulbus, however, it becomes firmly adherent to the sac, spreading out, fan-like, in its floor (fig. 4, B).

The inner sac is filled with a gelatinous coagulum, continuous with the vitreous body of the bulbus. After removal of this the sac is found to communicate with the bulbus through

a circular opening about 4 mm. in diameter. The optic nerve, as seen from above, spreads out in the floor and walls of the sac anteriorly and passes into the bulbus over the thickened, rounded rim of the opening.

The relation of the two sacs to the optic nerve and bulbus is schematized in figure 4. The inner sac appears to have been formed as an evagination of the pia, resulting undoubtedly from excessive intrabulbar pressure. Taking origin at the superior margin of the entrance of the optic nerve, this evagination had pushed out between the dura and pia of the nerve. By its expansion and the enlargement of the opening from the bulbus, the optic nerve became flattened anteriorly into a thin sheet attaching to the inferior and lateral edges of the opening. Posteriorly the nerve was subjected to less pressure and only slightly flattened between the dura and the inner sac, upon which its pia is reflected at the point where nerve and sac become adherent.

The bulbus is somewhat larger than that of a normal eye, though flattened considerably in its anteroposterior direction. The pupils are placed laterally; each has its own iris, cornea, and lens entirely distinct from that of the opposite side. There is, however, but one vitreous body, with no trace of a median septum.

DISCUSSION

The specimen above described illustrates in its structure the results of interference with growth changes fundamentally important in the development of the head. A few of these may be briefly noted, without, however, any attempt at a complete review of the literature on cyclopia.

Stockard ('09), in his well-known experiments with *Fun-
dulus*, has shown that a cyclopean condition may be readily induced through treatment of embryos with chemicals retarding development. From these results and from operations performed on *Amblystoma*, Stockard ('13) concludes that the entire eye primordium lies within a narrow median strip of medullary plate. From this, by lateral growth, the optic

outpocketings ultimately form; cyclopia, on the other hand, results when from any cause this lateral growth fails to occur. This interpretation emphasizes the conception that the single condition is the original or primary one, as opposed to the idea that cyclopia arises through fusion of originally separate anlagen.

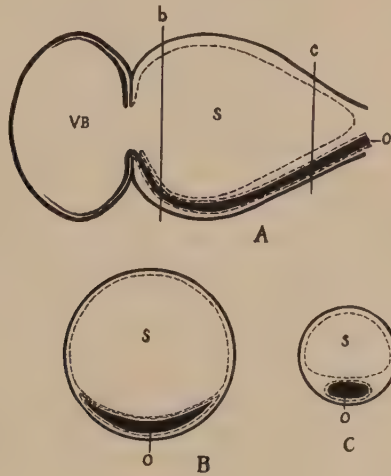


Fig. 4 Diagrams to show the relations of the bulbus oculi, optic nerve, and membranous sacs. The dura and the tunica fibrosa of the bulbus are represented by heavy lines, while the pia is indicated by dashes. A, a diagrammatic median sagittal section to show the continuity of the vitreous body with the contents of the closed pial sac. B and C, transverse sections of the sacs at the levels indicated by the lines *b* and *c* on A. O, optic nerve; S, pial sac; VB, vitreous body.

It is self-evident, I believe, that marked retardation of growth in the territory of optic primordium must of necessity affect the development of other structures in addition to the eye. According to Lewis ('09) and Stockard ('09), cyclopean *Fundulus* embryos usually develop with a normal brain. This, however, is far from being the truth as regards cyclopean mammals. In man, according to Mall ('17), "marked brain defects have always been found to accompany cases of cyclopia," and this statement holds for the writer's specimen.

We may safely assume that the failure of lateral growth leading to cyclopia is similarly responsible for the usual absence of olfactory lobes and cerebral hemispheres, the telencephalon remaining as a single vesicle. In the case described by Black ('13), in which such a 'forebrain vesicle' occurs, it contains "a well-marked hippocampal formation, while the rhinencephalon is entirely wanting." Mall states that in his embryo no. 559, "there is a ventral median defect of the brain . . . from the mamillary bodies to the front end of the brain. This defect naturally takes away the tissue between the eyes and between the cerebral vesicles. The eye stems have been taken out, olfactory lobes are absent, and the brain is reduced to a single vesicle."

On the basis of the experimental work of Stockard, conditions intermediate between that of Mall's embryo and the normal are understandable as expressions of growth failures, varying in degree, as a result of which median undifferentiated material fails to develop into the structures normally derived from it. Nothing has been 'cut out' or 'reduced' in the sense that it has been removed or destroyed by mechanical injury; structures are absent or modified simply because the growth of their primordia was checked at a critical stage in development.

Defects or complete absence of the median ventral structures of the forebrain in human cyclopia have been pointed out by Naegeli ('97), Black ('13), and Mall ('17). Similar defects unquestionably occur in the brains of other cyclopeans. The hippocampal formation, on the other hand, is stated by Naegeli and Black to be well developed. The most marked reduction of growth, therefore, would appear to have occurred at or close to the median line. From what we know of the early lateral expansion of the head it seems probable that this region is one of high metabolic activity and hence of high susceptibility. To this characteristic, doubtless, we owe the median defects of the brain, as well as the accompanying cyclopia.

Bilateral growth in the head is of course not limited to its ectodermal structures. Adelmann ('22) calls attention to the great bilateral growth of the prechordal mesoderm, "comparable to and coincident with the bilateral growth of the retinal areas" He points out that in the shark the premandibular head cavities are at first in communication across the midline. Later the lumen between the two cavities is obliterated, "and the resulting cellular cord (prechordal mesoderm) is drawn out to form a slender rod of cells which finally ruptures." In higher vertebrates, in which no head cavities appear, a comparable primary continuity of mesoderm ahead of the notochord nevertheless exists, and is similarly affected by lateral growth.

If, now, a marked failure of the usual early growth shiftings were to occur, the mesoderm of opposite sides would retain its primary prechordal continuity. As a result, the muscle masses derived from this mesoderm, those supplied by the third nerve, would from their earliest development be continuous from side to side; the masses innervated by the fourth and sixth nerves, on the other hand, would primarily never be joined with the corresponding masses of the opposite side.

This point is of extreme importance in understanding certain relations of the muscles in the cyclopean eye. The incomplete separation of those muscles innervated by the third nerves has been pointed out in the writer's material, in which inferior obliqui and recti form a single mass. A similar condition is reported by Wilder ('08) in a cyclopean pig (Teras VII), in which, however, the two inferior recti form one median mass, while the two inferior obliqui unite independently. In a human cyclops also described by Wilder (Teras VI), a single inferior muscle is present instead of the four evident in more complete doubling. The early human embryos, nos. 559 and 201, described by Mall, still possess an undifferentiated muscle mass crossing the median line; this is innervated by the third nerves. The 'fusion' or 'disappearance' of muscles innervated by the third nerves is of course but their

failure to separate from such a single mass; the latter, in turn, owes its unpaired condition to failure of the early bilateral growth changes characteristic of normal development.

The muscles supplied by the fourth and sixth nerves tend to be distinct from their fellows of the opposite side. A possible exception to this statement is furnished by Wilder's description of Teras VI, a human cyclops with fused muscles overlying the united inferior recti. Since Wilder did not trace the sixth nerve to these muscles, his statement that they represent lateral recti is open to question. If lateral recti, their fusion is probably secondary rather than primary, since the head cavities from which they originate in the lower vertebrates are not continuous across the midline as are those head somites supplied by the third nerves.

The fusion of the third nerves illustrated in figure 3 is of significance when considered in relation to the muscle masses they innervate. The retention of the early prechordal continuity of these masses permits the third nerves of opposite sides to effect an early anastomosis. This would be especially true in those cases in which the mesoderm had undergone the least bilateral growth. Mall's embryos nos. 559 and 201 show such an anastomosis already present in an early stage of embryonic life. Mall offers the comment that anastomosis of the third nerves appears as a constant feature of the cyclopean eye; his paper, however, does not show that he appreciated the full significance of this peculiarity.

The fourth nerves of opposite sides, as might be expected, are ordinarily not reported as forming anastomoses. Neither are the sixth. This condition is readily understood from the lack of primary continuity between the two muscle masses supplied by each pair of these nerves.

The inferior ocular muscles of figure 3 show another characteristic worthy of comment. I refer to their origin by numerous small tendons instead of the heads characteristic of the inferior recti. This, with other cases in the literature, may be taken to indicate the tendency to atypical division

and attachment of a muscle mass when its normal development is prevented. The parts shown in figure 3 are so little modified as to leave no question as to their derivation; this is further indicated by their innervation. In the specimen described by Black, on the other hand, modification of the orbit has resulted in the presence of several muscles of uncertain origin, which may be taken as an extreme result of the tendency pointed out above. Without the clues furnished by innervation such muscles must remain more or less a mystery as regards their origin.

In conclusion, it may be again emphasized that the various defects associated with cyclopia, as well as the cyclopean condition itself, are in large part the direct result of early growth failures or subsequent growth disturbances referable to an earlier growth failure as underlying cause. Their interpretation, therefore, must be in terms of reductions or failures of normal developmental processes rather than in terms of tissue destruction or secondary union of parts in the course of development. The latter processes need not be completely excluded, but the part they play is conceived as negligible in comparison with that played by altered growth processes; doubtless, too, it is limited largely to later developmental stages, after the defect has been very largely determined by a preceding growth failure.

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PLATE 1

EXPLANATION OF FIGURES

- 5 Lateral view of the specimen. $\times \frac{1}{2}$.
- 6 Frontal aspect, same magnification.
- 7 The eye. $\times 1\frac{1}{2}$. *P*, pupil.
- 8 Ventral aspect of the brain, approximately natural size. Cerebellum removed. *B*, basilar artery; *FB*, forebrain vesicle; *H*, hypophysis; *O*, olive; *I*, possible olfactory tract. Cranial nerves 2 to 10 are designated by Roman numerals.

